

N88 - 23373

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VAGAL TONE AS AN INDEX OF MENTAL STATE

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Overview.

Since autonomic processes such as heart rate are neurally mediated, it has been proposed that monitoring these variables will provide sensitive indicators of central nervous system status. Thus, many researchers have proposed that the neurally mediated oscillations in the heart rate pattern reflect a variety of mental states, including stress, emotion, consciousness or alertness, and attention. This paper will focus on the utility of monitoring oscillations in the heart rate pattern as a "window to the brain" and an index of general central nervous system status.

Heart rate in a healthy alert adult is not steady. The pattern of heart rate reflects the continuous feedback between the central nervous system and the peripheral autonomic receptors. The feedback produces phasic increases and decreases in neural efferent output via the vagus to the heart (ref. 1). In most situations like other measures of homeostatic function, the greater the range of the phasic increases and decreases, the "healthier" the individual. For example, with the aging process or with severe stress, there is an attenuation of the range of homeostatic function. Paralleling this process is a reduction in heart rate variability (ref. 2).

Thus, the efficiency of neural control may be manifested in rhythmic physiological variability and may portray the status of the individual and the individual's capacity and range to behave. In other terms, the greater the "organized" rhythmic physiological variability, the greater the range of behavior. Individuals with attenuated physiological variability, would then exhibit a lack of behavioral flexibility in response to environmental demands.

Although average heart rate seems to be a relative accurate index of metabolic activity, the topography of the heart rate pattern provides additional information regarding the continuous neural feedback between the cardiovascular system and the higher central nervous system structures. The spectral decomposition of the heart rate pattern identifies reliable oscillations at the respiratory frequency, at approximately .1 Hz hypothesized to reflect blood pressure feedback (e.g., Traube-Hering-Mayer wave, ref. 3), and at slower frequencies presumed to reflect thermoregulatory processes.

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Heart rate variability is a complex and often ambiguous construct. It has numerous mediators. The same level of heart rate variability can be mediated by a variety of combinations of neural and extra-neural influences. Therefore, our research has focused on respiratory sinus arrhythmia, the one oscillation in the heart rate pattern for which the physiological mechanisms are known.

It is possible to provide empirical evidence that the amplitude of respiratory sinus arrhythmia accurately maps into the efferent influence of the vagus nerve on the heart. It has been proposed that respiration, either by a central mechanism or via a peripheral feedback loop to medullary areas, phasically inhibits, or "gates" the source nuclei of the vagal cardio-inhibitory fibers (ref. 3). Maximal inhibition of vagal efferent output occurs during the mid to late inspiratory phase and maximal vagal efferent output occurs during the expiratory phase.

Recent research on neural pathways of vagal cardio-inhibitory neurons has demonstrated that the vagal cardio-inhibitory neurons show a respiratory-related pattern of discharge with the primary efferent action on the heart occurring during expiration (ref. 4). Data from electrophysiological studies have been so consistent that functional properties including bradycardia to neural stimulation, pulse rhythm, and firing primarily during expiration have been used to determine when a neuron is a vagal cardio-inhibitory neuron (ref. 5).

Given the above characteristics of vagal cardio-inhibitory neurons, a strong argument may be made that quantification of the amplitude of respiratory sinus arrhythmia provides an accurate index of cardiac vagal tone. Since the vagal cardio-inhibitory neurons, by definition, slow the heart rate and exhibit a respiratory frequency, the impact on heart rate should be slowing during the expiratory phase of respiration. The greater the vagal efferent output to the heart, the greater the slowing of heart rate during expiration. Thus, respiratory sinus arrhythmia is a peripheral manifestation of the influence of the vagal cardio-inhibitory neurons on the heart (i.e., cardiac vagal tone).

Physiological model.

Vagal tone is quantified by measuring the spontaneous rhythmic heart rate changes associated with respiratory activity. Functionally, the sensory information is transmitted to the respiratory control area of the medulla from the stretch receptors in the lungs - monitoring inhalation and exhalation - as well as information from the chemoreceptors in the cardiovascular system reflecting blood gas composition levels of oxygen and carbon dioxide. This information "tunes" the medullary respiratory drive frequency.

The respiratory center influences the output of the vagus as it conveys neural information to the heart. The vagal efferents are modulated by the respiratory center, producing an attenuation of vagal efferent influences to the heart during inspiration, and a reinstatement of vagal efferent influences to the heart during expiration. Thus, the

phenomenon is known as respiratory sinus arrhythmia. The amplitude of respiratory sinus arrhythmia is not constant, but reflects higher brain influences which directly inhibit or stimulate the cells of origin of the vagus. Changes in the amplitude of respiratory sinus arrhythmia can be observed in studies of sustained attention, stress, anesthesia, sleep state, and in response to pharmacological treatments which depress the central nervous system. During many of these conditions, the respiratory parameters remain relatively constant.

The Vagal Tone Measure.

Assessment of vagal tone necessitates accurate quantification of the amplitude of respiratory sinus arrhythmia. Only the component of heart rate variance associated with respiratory sinus arrhythmia can be both "physiologically" and "empirically" related to vagal influences to the heart. The most sensitive measures of vagal tone must be based upon these constraints. We have developed a time series approach which accurately extracts from the complex heart rate pattern the amplitude of respiratory sinus arrhythmia. This measure has been labeled V to emphasize it is a measure of vagal tone.

This procedure solves many of the problems associated with employing time series statistics to study physiological processes. These problems include non-stationarity, aperiodic influences, and the fact that even when physiological processes are periodic, such as breathing and respiratory sinus arrhythmia, they are not perfect sine waves. The method includes a series of mathematically derived steps designed to enhance the study of periodic processes. Information associated with sampling rate, heart rate, and breathing rate need to be known and are incorporated in the algorithms (ref. 6). The methods are based upon knowledge of physiology and statistics. Misunderstanding of the method, either from a statistical or physiological dimension, may result in an inappropriate application and uninterpretable data.

Other estimates of vagal influence, such as measures of total heart rate variability or mean successive differences, often reflect interesting relationships with health status and behavior. However, these measures are less sensitive to manipulations of vagal control and are less consistent in demonstrating relationships with situational and physiological variables. Moreover, these measures are confounded by both physiological constraints (e.g., non-vagal influences) and statistical aberrations (e.g., the sampling rate and the average heart rate influence the components of heart rate variability assessed with measures of heart rate variability that incorporate a successive difference approach). In many situations all measures of heart rate variability may be highly correlated, however, it can be demonstrated that the vagal tone measure is more sensitive to processes that can be physiologically linked to changes in parasympathetic tone.

These findings do not negate the importance of observations that global measures of heart rate variability are frequently related to mental states and clinical status. Rather, these points argue that global measures of heart rate variability are "composite" measures which can be

obtained through a variety of combinations of component influences on heart rate variability (such as movement, blood pressure feedback, respiratory sinus arrhythmia, and thermoregulatory influences). Therefore, it is impossible to make a strong statement regarding the specific physiological mechanisms mediating these relationships.

Validation studies.

To validate the vagal tone measure, a number of studies have demonstrated its sensitivity to manipulations of cardiac vagal tone (ref. 1). Our research has demonstrated that stimulation of the aortic depressor nerve in the rabbit increased the amplitude of respiratory sinus arrhythmia (ref. 7). Stimulation of the aortic depressor nerve produces a baroreceptor reflex characterized by increased vagal inhibitory action on the heart. Vagal blockade with atropine removed the effect. Propranolol, a beta-adrenergic blocker, did not alter the magnitude of the evoked increase in the amplitude of respiratory sinus arrhythmia. The amplitude of respiratory sinus arrhythmia was evaluated during manipulations of the baroreceptor reflex in anesthetized cats (ref. 8). Hypertension, induced by infusion of nitroprusside, was used to inhibit cardiac vagal tone. The manipulations effectively produced state changes in blood pressure and reflexively influenced the cardio-inhibitory influence on the heart (i.e., vagal tone). Hypertension produced an increase in the amplitude of respiratory sinus arrhythmia. Hypotension produced a decrease in the amplitude of respiratory sinus arrhythmia. Specific autonomic contributions were assessed with administration of practolol (a beta-adrenergic blocker) and atropine.

Although the above studies were conducted in anesthetized preparations, we also have conducted research with alert and moving preparations. In a study with rats, phenylephrine increased, atropine abolished, and saline had no effect on the amplitude of respiratory sinus arrhythmia (ref. 9). In a study with alert adults, four treatment levels of atropine and a placebo control were administered (ref. 10, ref. 11). The data demonstrated that the vagal blockade was monotonically related to the amplitude of respiratory sinus arrhythmia. Moreover, respiratory sinus arrhythmia was more sensitive to vagal blockade than heart rate (the change in heart rate in response to atropine is often used a criterion measure of vagal tone).

Sustained attention.

In a number of studies (ref. 12, ref. 13, ref. 14), heart rate variability was evaluated during a variety of attention demanding tasks. These studies demonstrated that independent of the direction of the heart rate change during the tasks, heart rate variability was consistently suppressed during sustained attention. Moreover, individuals with higher baselevel heart rate variability exhibited greater suppression of heart rate variability and performed better on reaction time tasks. These studies used a measure of overall heart rate variability and were conducted before the statistical procedures were developed to extract the amplitude of respiratory sinus arrhythmia.

Recently we have conducted research on the vagal tone measure during sustained attention. In this study physiological and performance measures were evaluated on 30 male and female students with a mean age of 20.2 years. The tasks were mental arithmetic and a tracking presented via an Atari Videoarcade system. Both tasks contained timers that were visibly displayed and that counted down while the subject tried to accumulate as many laps (in the tracking task) or points (in the arithmetic task).

For the tracking task, the subject was asked to race a video representation of a car around a track to make as many laps as possible in 60 sec. The task contained an element of uncontrollability. The task was designed so that there was a tradeoff between speed and accuracy. If the car went too fast for a certain period of time, the car would veer off course into the progress-impeding borders. The task required being able to control the speed while skillfully guiding the car to avoid the time-consuming border areas. Subjects were told that psychomotor skill was being assessed and that they would receive five cents for every completed lap. Subjects were given a practice session. The 60-second task was followed by a 60-second rest period referred in the figures as the "off-task" period. Each subject received three trials of an on-task/off-task sequence.

In the arithmetic task, five numbers between 1 and 9 were presented on the video screen for five seconds. A timer, displayed in the center of the screen, counted down while the subject tried to add the numbers together. Subjects responded by pressing a button. Subjects were rewarded for performance. Similar to the "race," the "sum" task was presented in three one-minute trials of an on-task/off-task sequence.

Collapsed across tasks heart period was shorter (faster heart rate) on task (748 msec) than off-task (850 msec); heart period variability was lower on-task (7.8) than off-task (8.4); respiratory frequency was faster on task (.33 hz) than off-task (.25 Hz); Vagal tone was lower on-task (7.4) than off-task (8.9); and the .1 Hz wave had lower amplitude on-task (7.3) than off-task (7.7).

A quantitative method of assessing the relative sensitivity of the above dependent variables to attention demands is to calculate eta or omega squared for the on-task/off-task effect. This procedure assesses the percentage of variance of the dependent variable mediated by the tasks. If the physiological variable is sensitive to the attention demands, it will be reflected in a greater percentage of the sums of squares associated with task relative to the total sums of squares in the analysis of variance table. The vagal tone index was the most sensitive of the physiological variables with an eta of .24 (i.e., 24% of the variance of vagal tone was mediated by the attention demanding tasks). The amplitude of the .1 Hz wave (i.e., Traube-Hering-Mayer wave), which has been reputed to be sensitive to sustained attention had the lowest eta and accounted for only 8% of the variance.

Flight performance and vagal tone.

The study by Dellinger, Taylor, and Porges (1987) (ref. 10) provides data on the relationship between changes in vagal tone and flight performance decrement. The injection of atropine resulted in significant performance decrements beginning at 1 hour post-injection and only minimal recovery by post-injection. In contrast, the decrement in vagal tone was almost instantaneous. The early physiological symptoms that occur prior to the performance decrements potentially could be used in bio-cybernetic system to allow the pilot to land safely.

Thus, although there is a parallel under the high doses of atropine (2.0 mg/75 kg, 4.0 mg/75 kg) between vagal tone and pilot performance, the time courses of the two classes of variables differ. The vagal tone measure reflects the immediate influence on the physiology although performance does not deteriorate for at least one hour, thus reflecting the pilot's ability to compensate.

Summary.

Other influences on central nervous system such as anesthesia, head trauma and sleep have been investigated. For example, inhalant anesthesia which blocks central nervous system monitoring of peripheral sensory information virtually eliminates vagal tone. The vagal tone monitored following head trauma in the intensive care unit predicts neurological outcome. Other studies have demonstrated that vagal tone shifts as a function of sleep state. In general the vagal tone index appears to monitor global states of the central nervous system and may be useful in screening the general state of pilots.

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